**Introduction:** Cardiac cachexia is a common complication of congestive heart failure (CHF) and is associated with poor prognosis. Patients with cardiac cachexia suffer from generalized loss of lean tissue, fat tissue, as well as bone tissue. Aldosteronism in congestive heart failure contributes to both a salt-avid state and a systemic illness that features oxidative/nitrosative stress and a proinflammatory phenotype with tissue wasting, including bone.

It has been shown that spironolactone, an aldosterone receptor antagonist, can prevent bone loss in hyperandrogenic women treated with gonadotropin-releasing hormone agonist (GnRHa), and reverse rickets changes in a child with 11 beta-hydroxysteroid dehydrogenase deficiency. This suggests that osteopenia could be a consequence of excessive mineralocorticoid activity. We have previously shown severe osteopenia in ALDOST rats with a profound reduction in femoral bone strength and bone mineral density (BMD) along with a marked urinary loss of Mg2+ and Ca2+. Spironolactone successfully reduced bone loss in this experimental model, providing evidence for a role for aldosterone in bone loss and a potential treatment for osteopenia in patients with cardiac cachexia. In the present study we examined the effects of spironolactone and salbutamol ($\beta_2$-adrenergic receptor agonist with potential anabolic properties) treatments on bone compared to rats allowed to recover from ALDOST.

**Materials and Methods:** Male, 8-week-old Sprague-Dawley rats were uninephrectomized and continuously received aldosterone (0.75 μg/h) using an implanted subdermal minipump together with 1% NaCl/0.4% KCl in drinking water (ALDOST) and standard laboratory chow containing 1.13% Ca2+ and 0.24% Mg2+. After four weeks of ALDOST, one group was allowed to recover for four weeks and the other two groups remained on aldosterone and simultaneously treated with either spironolactone via gastric lavage (75mg/rat/day) or salbutamol (200 mcg/day IP). Rats were euthanized 8 weeks after surgery. This protocol was approved by the University of Tennessee Health Science Center Animal Care and Use Committee.

Both 2-D and 3-D BMD were determined for excised, soft tissue-cleaned femurs by dual-energy X ray absorptiometry (DEXA) using a GE Lunar PIXImus2 and an ImTek (Siemens) MicroCT, respectively. An Instron Universal Test System was used for the three-point bending test to determine the flexure stress of rat femoral diaphyses.

All values are presented as mean ± SEM. Data were analyzed using analysis of variance. Significant differences between individual means were determined using the post hoc Bonferroni multiple comparisons test. Significance level was assigned to 0.05.

**Results:**

Spironolactone successfully kept BMD comparable to the recovery group, however bone strength was less compared to the recovery group but still significantly different from Spironolactone n = 10, Spironolactone n = 6) * = significantly different from Recovery; + = significantly different from Spironolactone

Femurs from the salbutamol treated group had significantly less BMD than either the recovery or spironolactone group for both 2-D and 3-D measurements (p < 0.05) (Figures 1&2). There was no significant difference between the BMDs of the spironolactone and recovery groups (p > 0.05). The mechanical data, in agreement with the BMD data, showed a significant decrease in flexure stress of femurs in the salbutamol group compared to the recovery and the spironolactone group (Figure 3). However, unlike the BMD data, the spironolactone group femurs demonstrated significantly less flexure stress than the femurs from the recovery group, although still significantly more strength than the salbutamol group femurs.

**Discussion:** Spironolactone successfully kept BMD comparable to the recovery group, however bone strength was less compared to the recovery group but still greater than the salbutamol group femurs. Salbutamol proved unsuccessful in recovering BMD loss or bone strength compared to the recovery group. These data suggest a role for aldosterone in bone loss and provide a potential treatment for osteopenia in cardiac cachexia patients with spironolactone. Other treatments, such as dietary supplement of calcium and vitamin D, bisphosphonates, and calcitonin are worthy of further study.

**References:**